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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,125	10/27/2005	Yuji Hayashi	868_006	1475

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EXAMINER	
HA, JULIE	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,125	HAYASHI ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 27, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *2-6,12 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7-11,13 and 16* is/are rejected.

7)☒ Claim(s) *15 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment filed on December 27, 2006 is acknowledged. Claims 1-17 are pending in this application.

Election/Restriction

1. Applicant's election of species (1) a peptide as recited in claim 1, wherein W_{aa} and X_{aa} are Lys, Y_{aa} is Arg or Arg-NH2, and n is an integer of 1 to 9 (specific peptide species (2), SEQ ID NO:15) in the reply filed on December 27, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 3-6, 12 and 14 are withdrawn from consideration drawn to nonelected species. Claims 9-11 will be examined only on elected species.

2. Search was performed for SEQ ID NO: 15. The SEQ ID NO was deemed to be free of prior art. Search was then extended as stated in MPEP § 803.02: "Should the examiner determine that the elected species is allowable, the examination of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species." For Markush type claim 1, prior art was found that anticipated claim 1. Since prior art reads on claims 1, 7-11, 13 and 16, those claims have been rejected and claims 2, 4 and 5 are hereby withdrawn as corresponding to

nonelected species in addition to claims 3, 6, 12 and 14 (thus, claims 2-6, 12 and 14 are withdrawn). Claims 15 and 17 are free of prior art. Claims 1, 7-11, 13 and 15-17 have been examined on the merits in this application.

Objection-Specification

3. The abstract of the disclosure is objected to because the abstract is limited to 1 paragraph and may not exceed 150 words in length. Correction is required. See MPEP § 608.01(b).

4. The title of the Invention is objected to because the title is too long. The title is limited to 5-7 words in length. Correction is required.

Rejection-35 U.S.C. 112, 2nd

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. In claims 1, 7 and 9 the language "one or a few amino acids" is unclear. Since the claim is drawn to a peptide comprising an amino acid sequence of GLP-1(7-35) or of GLP-1(7-35) having deletion, substitution and/or addition of one or a few amino acids, it is unclear how the sequence can have addition of one or a few amino acids and still maintain the length of a GLP-1(7-35).

Rejection-35 U.S.C. § 112, 1st

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 7-9, 13 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

10. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties,

functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

11. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

12. The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative

number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

13. In the instant case, the claims are drawn to a peptide comprising an amino acid sequence of GLP-1(7-35) or of GLP-1(7-35) having deletion, substitution and/or addition of one or a few amino acids. The generic statements deletion, substitution and/or addition do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

14. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule, and all derivatives. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since

the specification does not provide any examples of derivatives. The specification is void of where these deletions, substitutions and additions of one or a few amino acids are.

15. The specification is limited to substitution at position 8 with serine (see paragraph [0020]). Moreover, the working example only discloses the activity of GLP-1 derivative 8S26Q34N-GLP-1 (substitution at 8, 26 and 34th positions) (see paragraph [0058]). There are so many different variants of GLP-1 peptides with variable substitutions, additions and deletions that can be applied to the peptide. The specification does not describe peptide derivatives besides these two described substitutions. For example, US Patent # 69031586 discloses GLP-1 peptides having substitutions at the 35th position (see SEQ ID NO: 49). This patent discloses multiple GLP-1 peptide variants (see for example columns 27 and 28). Description of substitution at positions 8, 26 and 34 is not sufficient to encompass the numerous varying lengths to be significant amount of examples.

16. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Rejection-35 U.S.C. 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1, 7-11, 13, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Dong ZX (US Patent # 6903186).

19. The instant claims are drawn to a pharmaceutical composition comprising as an active ingredient a peptide comprising an amino acid sequence of GLP-1(7-35) or of GLP1(7-35) having deletion, substitution and/or addition of one or a few amino acids and having a GLP-1 activity with Waa-(Xaa)n-Yaa (where Waa is Arg or Lys, Xaa is the same with Waa, n is an integer of 0 to 14, and Yaa is Arg or Arg-NH_2) on its C-terminus of the peptide. The claims are further drawn to a pharmaceutical composition used for nasal administration, which contains a fat emulsion, and used in treatment of non-insulin dependent chronic diabetes mellitus.

20. Dong ZX teaches peptide analogs of GLP-1, the pharmaceutically acceptable salts thereof, to methods of using such analogues to treat mammals and to pharmaceutical compositions useful therefore for comprising the analogues (see abstract). This reads on claim 8. The reference teaches SEQ ID NO: 49, the sequence of GLP1(7-37), wherein the 36^{th} and 37^{th} amino acids are Arg and Arg (see SEQ ID NO: 49, column 69). Since n can be 0, this reads on claims 1, 8, 13 and 16. The reference further teaches that the GLP-1 was suggested following the observation that a single

subcutaneous dose of GLP-1 could completely normalize postprandial glucose levels in patients with non-insulin-dependent diabetes mellitus (see column 1, lines 41-45). This reads on claims 11 and 16. The reference further teaches that the compounds can be administered by oral, parenteral, nasal, vaginal, rectal and so on (see column 13, lines 23-26); preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, or emulsions (see column 13, lines 37-39); liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solution, suspensions, syrups and so on (see column 13, lines 30-32). Additionally, the reference teaches that compositions for nasal or sublingual administrations are also prepared with standard excipients well known in the art (see column 13, lines 56-57). Although the prior art is silent as to transmucosal administration, it is inherent to the artisans in the field that nasal administration is transmucosal administration. Therefore, this meets the limitations of claims 7-10.

Allowable Subject Matter

Objection-Claims

21. Claims 15 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

22. Claims 15 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 1, 7-11, 13 and 16 are rejected. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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